Whole Grain Intake Is Associated with Lower Body Mass and Greater Insulin Sensitivity among Adolescents

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The authors tested the hypothesis that consumption of whole grain is associated with greater insulin sensitivity and lower body mass index (BMI) (weight (kg)/height (m)²) in adolescents and that this association is stronger among the heaviest adolescents. Two 127-item food frequency questionnaires were administered at the mean ages of 13 years (standard deviation 1.2) and 15 years (standard deviation 1.3) to 285 Minnesota adolescents who underwent two euglycemic insulin clamp studies 2 years apart as part of a protocol evaluating the influence of insulin resistance on development of adverse cardiovascular disease risk factors. Intake of whole grain was examined for associations with BMI and insulin sensitivity (measured as milligrams of glucose uptake per kilogram of lean body mass (Mlbm) per minute). After adjustment for age, gender, race, Tanner stage, and energy intake, mean BMI was 23.6 for adolescents consuming less than ½ serving/day of whole-grain foods, 22.6 for ½–1½ servings/day, and 21.9 for more than 1½ servings/day (p = 0.05). After adjustment for age, gender, race, Tanner stage, energy intake, BMI, and physical activity, M lbm was 11.6, 12.3, and 13.2 mg/kg/minute, respectively, in the three whole grain intake groups (p = 0.02). This relation was stronger among adolescents with higher BMIs (ρ = 0.001). Whole grain intake was associated with greater insulin sensitivity and lower BMI in adolescents, especially among the heaviest persons.

adolescence; body mass index; cardiovascular diseases; cereals; insulin; insulin resistance; risk factors

Abbreviations: BMI, body mass index; SD, standard deviation.

An alarming increase in type 2 diabetes mellitus among children and adolescents has emerged (1, 2) at the same time that national surveys have shown a trend towards an increasing prevalence of overweight and obesity in the US population (3). Increased body mass index (BMI) is a common factor in insulin resistance, a precursor for type 2 diabetes. Data from our study (4) and others (5–10) have shown that insulin resistance is associated with the clustering of adverse cardiovascular disease risk factors, including increased levels of high BMI/obesity, triglycerides, insulin, glucose, and systolic blood pressure and low levels of high density lipoprotein cholesterol, in children and adults.

Consumption of whole grain is associated with a lower risk of developing cardiovascular disease, diabetes, and hypertension in adults (11–14). Additionally, whole grain consumption is inversely related to BMI, waist circumference, and fasting insulin level (12, 13). Reduced body mass with higher whole grain intake may be mediated in part by enhanced insulin sensitivity and increased satiety in consumers of whole grain (15–17). Whole grains are rich in a myriad of nutrients and food compounds, including vitamins (particularly vitamin E), minerals, complex carbohydrates, dietary fiber, phytochemicals, and other substances that have been related to body weight regulation and reduction of insulin resistance and cardiovascular disease risk factors (18). Findings from the 1994–1996 Continuing Survey of Food Intake in Individuals showed that US adults consumed an average of 6.9 servings of grain products per day, but only one serving per day was whole grain (19). Only 8 percent of adults consumed three or more servings of whole-grain foods per day (19), the recommended amount according to the Dietary Guidelines for Americans (20).
Corresponding information for children and adolescents is not available. In a market research study, adolescents and adults reported consuming whole-grain foods an average of 0.4 and 0.5 times per day, respectively, during a 2-week period (21).

To our knowledge, the relation of whole grain intake to insulin sensitivity and cardiovascular disease risk factors has not been studied in adolescents. Therefore, we analyzed data from a cohort of adolescents to test the hypothesis that whole grain intake is associated with lower BMI, greater insulin sensitivity, and an improved cardiovascular disease risk factor profile. Because the association of whole grain intake with insulin sensitivity and reduced risk of type 2 diabetes was observed to be stronger in an overweight adult population (13), we hypothesized that this association would also be stronger in adolescents with higher BMIs.

MATERIALS AND METHODS

Study population

The adolescents in this study included 357 Minneapolis, Minnesota, students in the fifth to eighth grades who were selected by stratification on gender, race, and systolic blood pressure criteria after they participated in a blood pressure screening program conducted in the Minneapolis public schools (22). Of the 357 adolescents, 285 (155 boys and 130 girls) had completed two insulin clamp studies 2 years apart and filled in two food frequency questionnaires coincident with the clamp studies; these students formed the cohort for this study. The study protocol was approved by the Institutional Review Board: Human Subjects Committee of the University of Minnesota. Consent was obtained from all children and their parents/guardians after the purpose and possible risks of the study had been described.

Measurements

Physical examination. Height was measured using a wall-mounted stadiometer. Weight was determined using a balance scale. BMI was computed as weight (kg) divided by height squared (m²). Triceps and subscapular skinfold thicknesses were measured twice to the nearest millimeter with Lange calipers, and the mean of the two measurements was used in the analyses. Lean and fat body mass were calculated using the Slaughter equations (23). Waist circumference was measured to the nearest 0.5 cm. Tanner stage was assessed by a pediatrician. Children were classified into Tanner stages according to pubic hair development in boys and breast and pubic hair development in girls. In girls, the greater of the two values was used for statistical analysis so that maturation would not be underestimated. Blood pressure was measured twice on the right arm using a random-zero sphygmomanometer with the subject seated; the average of two measurements was used in the analyses. The average of two measurements of each of systolic blood pressure and fifth-phase Korotkoff diastolic blood pressure was used in the analyses.

Euglycemic insulin clamp. Insulin sensitivity was determined by the euglycemic insulin clamp method, in which insulin was infused at a rate of 1 mU/kg/minute for 3 hours. A variable infusion of 20 percent dextrose was used to maintain the serum glucose level at 100 mg/dl. Blood glucose concentration was measured every 5 minutes. Insulin levels were measured at baseline (15, 10, and 5 minutes before the infusion was begun) and at steady state (140, 160, and 180 minutes after the infusion was started). Insulin sensitivity was expressed as $M_{\text{inf}}$, where $M$ is milligrams of glucose utilization per kilogram of lean body mass (lbm) per minute (24).

Laboratory measurements. Blood samples were analyzed for glucose immediately at the bedside with a Beckman Glucose Analyzer II (Beckman Instruments, Inc., Fullerton, California). The insulin samples were collected on ice and centrifuged within 20 minutes. Insulin levels were determined using a radioimmunoassay kit (Equate RIA, Binax Corporation, Portland, Maine). The average of the three baseline measurements was used in the analyses. Blood samples for determination of serum lipid levels were analyzed in the University of Minnesota hospital laboratory using a Cobas FARA analyzer (Roche Diagnostic Systems, Inc., Branchburg, New Jersey). Cholesterol levels were determined using a standard enzymatic cholesterol oxidase-based method; high density lipoprotein cholesterol level was determined after precipitation of non-high density lipoproteins with magnesium/dextran precipitating reagent. Low density lipoprotein cholesterol level was calculated according to the Friedewald equation. Triglyceride levels were determined using a standard glycerol blanked, enzymatic triglyceride method.

Assessment of physical activity. A modified Paffenbarger physical activity questionnaire was administered to the adolescents at baseline and 2 years later (25). Total energy expenditure was estimated according to an algorithm (26).

Assessment of dietary intake. The 127-item Willett food frequency questionnaire was administered to the adolescents by an interviewer, with parental help, at baseline and 2 years later (27). Although this questionnaire was not validated in this population, a similar questionnaire has been validated in youth (28), and energy intakes and percentages of calories from fat, carbohydrate, and protein were similar to those reported in other adolescent populations (28, 29). Participants were asked to report the frequency of consumption of each food from nine categories, ranging from never or less than once per month to six or more times per day. Interviewers also obtained additional information, including the type of breakfast cereal usually consumed, other foods regularly consumed, and intake of vitamin supplements.

Food grouping. Foods were classified into seven groups: dairy foods, meat, fish, poultry, fruit and vegetables, whole grains, and refined grains. The whole- and refined-grain groups were formed according to procedures previously developed (30). Whole-grain ready-to-eat breakfast cereals contained at least 25 percent whole grain or bran by weight, as determined from the package label or from records shared by cereal manufacturing companies. Other food items classified as whole-grain included cooked oatmeal, dark bread, brown rice, other grains (bulgur, kasha, couscous), bran, wheat germ, and popcorn. Refined-grain food items included ready-to-eat breakfast cereals with less than 25 percent whole grain or bran, white bread, bagels, rolls, muffins, pasta, white rice, pancakes and waffles, doughnuts, cake, cookies and bars, and pie.
Although the food frequency instrument was not designed initially to differentiate whole-grain foods from refined-grain foods, any misclassification of foods would have resulted in an attenuated association. For example, hot cereals were classified as a refined-grain food; therefore, any association would be underestimated if some whole-grain hot cereals (other than oatmeal, a whole-grain cereal that was queried about separately) were actually included in the food group labeled refined-grain. The Spearman correlation coefficients for correlation between the food frequency questionnaire administered at baseline and the questionnaire administered 2 years later were as follows: whole-grain foods, 0.39; refined-grain foods, 0.21; fruit, 0.35; vegetables, 0.47; meat, 0.46; and dairy foods, 0.36. All were statistically significant ($p < 0.001$).

**Statistics**

All analyses were conducted with the statistical software package SAS, version 8.1 (SAS Institute, Inc., Cary, North Carolina). Spearman partial correlation coefficients were calculated and adjusted for age, gender, race, Tanner stage, and total energy intake. We adjusted for Tanner stage because, in this cohort, insulin resistance increased between Tanner stages 1 and 2, remained stable through Tanner stages 2, 3, and 4, and decreased at Tanner stages 5 (22). Tanner stage was based on the assessment made at the baseline examination, because over 80 percent of the adolescents were Tanner stage 4 or 5 at the examination 2 years later. In a sensitivity analysis, we further adjusted for change in Tanner stage (no change, change from stage 1 to stage 2 or greater ($n = 20$), and change from stage 2 to 3 to stage 4 or 5 ($n = 85$)); this further adjustment had essentially no effect on the association between insulin sensitivity and whole-grain intake (data not shown). Age at baseline was used for adjusting the regression models. To increase precision in our initial analyses of these data, data on all variables except age and Tanner stage were averaged across the 2 years. In sensitivity analyses, data were also analyzed as prospective longitudinal data using the PROC MIXED procedure in SAS. Similar results were observed as for the cross-sectional analysis, although the relations were not statistically significant because of inadequate power (data not shown). Multiple regression analyses (PROC GLM) were performed using each of BMI, fat body mass, lean body mass, fasting insulin, insulin sensitivity, and other cardiovascular disease risk factors as dependent variables and intake of whole-grain foods as the independent variable, adjusting for age, gender, race, Tanner stage, total energy intake, BMI, and physical activity as indicated.

**RESULTS**

The cohort was 86 percent Caucasian and 14 percent African-American. Overall, 46 percent of the students were female and 54 percent were male. Their physical and clinical characteristics are shown in table 1. The mean age of both girls and boys at baseline was 13 years. The average Tanner stage at baseline was slightly greater than 3. Mean BMIs for girls and boys were 22.9 and 22.4, respectively. As expected, girls had a higher fat mass than boys, but boys had greater lean mass and were more insulin-sensitive than girls. Boys consumed more calories per day than girls, although both boys and girls consumed approximately 55 percent of their daily calories from carbohydrate, 15 percent from protein, and 30 percent from total fat. Comparison of average nutrient intakes with Dietary Reference Intakes found the adolescents’ diets to be nutritionally adequate for iron, zinc, folate, and vitamin E (data not shown). However, average calcium intake was slightly low for girls (1,240 mg/day), while boys consumed greater than the recommended 1,300 mg/day. Most adolescents (82 percent of boys and 75 percent of girls) did not consume vitamin and mineral supplements. Both girls and boys consumed slightly less than 1½ servings of whole-grain foods per day.

Table 2 provides the average number of servings of food consumed per day from each food group, categorized across tertiles of whole-grain consumption, with adjustment for age, gender, race, Tanner stage, and energy intake. Similar numbers of servings were consumed from the refined grain and dairy food groups across the three whole-grain categories. The number of servings of fruit and vegetables consumed per day increased with greater consumption of whole-grain foods. In contrast, the number of servings of meat consumed per day was lower with greater consumption of whole-grain foods. Favorable associations of iron, zinc, calcium, folate, and vitamin E were observed across tertiles of whole-grain consumption (data not shown). Physical activity was also positively related to whole-grain intake.

Spearman partial correlation coefficients were calculated and adjusted for age, gender, race, Tanner stage, and total energy intake. Insulin sensitivity (M lbm) was significantly and inversely related to BMI ($r = -0.20; p = 0.001$). Whole grain intake was inversely associated with BMI ($r = -0.14; p = 0.01$) and directly associated with M lbm ($r = 0.18; p = 0.004$). It was not significantly related to fasting insulin level ($r = -0.09; p = 0.14$). Refined grain intake was not significantly related to BMI, insulin sensitivity, or fasting insulin (data not shown).

Table 3 displays the relation of body size, insulin measures, and cardiovascular disease risk factors with tertile of whole-grain intake, adjusted for age, gender, race, Tanner stage, and energy intake. There were inverse dose-response relations of both BMI and waist circumference with whole-grain intake ($p = 0.05$ and $p = 0.02$, respectively). The BMI difference corresponds to approximately a 5-kg difference between the first and third tertiles of whole-grain intake. As is noted in the table, almost all of the difference in BMI is attributed to fat mass and not lean mass.

Insulin sensitivity (M lbm) had a positive dose-response association with whole grain intake ($p = 0.01$), as table 3 shows. This association remained significant after further adjustment for BMI and physical activity ($p = 0.03$) (see figure 1). Fasting insulin was inversely related to whole grain intake, but this was not statistically significant ($p = 0.07$), and further adjustment for BMI and physical activity weakened this relation ($p = 0.41$). When a continuous interaction term was included in the model, the relation between M lbm and whole grain intake was stronger among adolescents with higher BMIs ($p$ for interaction $= 0.001$).
prominent feature of this interaction was observed in the 40 children with BMIs greater than or equal to 27.5. (This cutpoint was selected arbitrarily to illustrate how the relation of Mlbm with whole grain intake strengthened as BMI increased.) Among the 17 children who ate less than ½ serving/day of whole grain, mean Mlbm was 8.5 mg/kg/minute (standard deviation (SD) 0.85); among the 14 children who ate ½–1½ servings/day of whole grain, mean Mlbm was 11.8 mg/kg/minute (SD 0.94); and among the nine children who ate more than 1½ servings/day of whole grain, mean Mlbm was 13.6 mg/kg/minute (SD 1.2). In other words, Mlbm was lower among the fatter children consuming less than ½ serving of whole-grain foods daily (8.5 mg/kg/minute) than among lean children (12.4 mg/kg/minute).

Although one would expect that Mlbm would be lower among all of the fatter children in comparison with lean children, Mlbm’s were similar among both fatter children and lean children consuming 1½ servings of whole-grain foods per day (13.6 mg/kg/minute vs. 13.2 mg/kg/minute, respectively). There was a parallel finding for fasting insulin level (p for interaction < 0.001) among the 40 children with BMIs greater than or equal to 27.5: mean fasting insulin was 31.4 mU/liter (SD 1.7) in the 17 children who ate less than ½ serving of whole grain, 21.0 mU/liter (SD 1.9) in the 14 children who ate ½–1½ servings per day, and 19.5 mU/liter (SD 2.3) in the nine children who ate more than 1½ servings per day.

Table 3 also shows mean values for cardiovascular disease risk factors by tertile of whole grain intake, adjusted for age,
### TABLE 2. Adjusted mean daily dietary intakes by tertile of whole grain intake among 285 adolescent students in Minneapolis, Minnesota, 1996–1999

<table>
<thead>
<tr>
<th>Characteristic†</th>
<th>Whole grain intake (no. of servings/day)</th>
<th>&lt;½ (n = 76)</th>
<th>½–1½ (n = 117)</th>
<th>&gt;1½ (n = 91)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily nutrient intake</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td></td>
<td>2,292</td>
<td>81</td>
<td>2,250</td>
<td>65</td>
</tr>
<tr>
<td>Protein (g)</td>
<td></td>
<td>90.3</td>
<td>1.8</td>
<td>92.7</td>
<td>1.5</td>
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<tr>
<td>Total fat (g)</td>
<td></td>
<td>84.6</td>
<td>1.5</td>
<td>81.8</td>
<td>1.2</td>
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<tr>
<td>Carbohydrate (g)</td>
<td></td>
<td>335.6</td>
<td>4.5</td>
<td>340.9</td>
<td>3.6</td>
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<tr>
<td>Total fiber (g)</td>
<td></td>
<td>16.4</td>
<td>0.5</td>
<td>18.6</td>
<td>0.4</td>
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<tr>
<td>Food group intake (no. of servings/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whole grain</td>
<td></td>
<td>0.4</td>
<td>0.1</td>
<td>1.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Refined grain</td>
<td></td>
<td>3.1</td>
<td>0.2</td>
<td>3.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Fruit/vegetables</td>
<td></td>
<td>5.2</td>
<td>0.3</td>
<td>6.0</td>
<td>0.2</td>
</tr>
<tr>
<td>Meat</td>
<td></td>
<td>1.8</td>
<td>0.1</td>
<td>1.7</td>
<td>0.1</td>
</tr>
<tr>
<td>Dairy foods</td>
<td></td>
<td>3.8</td>
<td>0.2</td>
<td>3.9</td>
<td>0.2</td>
</tr>
<tr>
<td>Physical activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy expenditure (kcal/day)</td>
<td></td>
<td>702</td>
<td>60</td>
<td>664</td>
<td>49</td>
</tr>
</tbody>
</table>

* Adjusted for caloric intake, age, gender, race, and Tanner stage, except energy intake, which was adjusted for age, gender, race, and Tanner stage.
† All variables were averaged for visits 1 and 2.
‡ SE, standard error.

### TABLE 3. Adjusted mean values for cardiovascular disease risk factors by tertile of whole grain intake among 285 adolescent students in Minneapolis, Minnesota, 1996–1999

<table>
<thead>
<tr>
<th>Characteristic†</th>
<th>Whole grain intake (no. of servings/day)</th>
<th>&lt;½ (n = 76)</th>
<th>½–1½ (n = 117)</th>
<th>&gt;1½ (n = 91)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index§</td>
<td></td>
<td>23.6</td>
<td>0.53</td>
<td>22.6</td>
<td>0.43</td>
</tr>
<tr>
<td>Fat mass</td>
<td></td>
<td>8.0</td>
<td>0.51</td>
<td>7.2</td>
<td>0.42</td>
</tr>
<tr>
<td>Lean mass</td>
<td></td>
<td>15.7</td>
<td>0.19</td>
<td>15.5</td>
<td>0.16</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td></td>
<td>81.4</td>
<td>1.23</td>
<td>78.3</td>
<td>1.00</td>
</tr>
<tr>
<td>Clinical characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting insulin level (mU/liter)</td>
<td></td>
<td>16.7</td>
<td>0.95</td>
<td>14.4</td>
<td>0.77</td>
</tr>
<tr>
<td>Insulin sensitivity¶ (mg/kg/minute)</td>
<td></td>
<td>11.5</td>
<td>0.42</td>
<td>12.3</td>
<td>0.34</td>
</tr>
<tr>
<td>Fasting glucose level (mg/dl)</td>
<td></td>
<td>99.4</td>
<td>0.74</td>
<td>99.0</td>
<td>0.60</td>
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<tr>
<td>Systolic blood pressure (mmHg)</td>
<td></td>
<td>109.3</td>
<td>0.95</td>
<td>108.2</td>
<td>0.77</td>
</tr>
<tr>
<td>Cholesterol level (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td></td>
<td>152.7</td>
<td>3.14</td>
<td>147.6</td>
<td>2.56</td>
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<tr>
<td>HDL cholesterol</td>
<td></td>
<td>43.8</td>
<td>1.04</td>
<td>42.7</td>
<td>0.84</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td></td>
<td>90.4</td>
<td>2.73</td>
<td>86.8</td>
<td>2.22</td>
</tr>
<tr>
<td>Triglyceride level (mg/dl)</td>
<td></td>
<td>90.7</td>
<td>5.38</td>
<td>92.0</td>
<td>4.38</td>
</tr>
</tbody>
</table>

* Adjusted for energy intake, age, gender, race, and Tanner stage.
† All variables were averaged for visits 1 and 2.
‡ SE, standard error; HDL, high density lipoprotein; LDL, low density lipoprotein.
§ Weight (kg)/height (m)².
¶ Milligrams of glucose utilization per kilogram of lean body mass per minute.
gender, race, Tanner stage, and energy intake. Associations of whole grain with these risk factors were essentially unchanged when fruits and vegetables, meat, and dietary fiber were included in the models.

Figure 2 depicts gender-specific patterns of the relations of BMI and Mlbm with whole grain intake. Though not significant, the same relations held true as for the whole group: BMI was lower and Mlbm was higher with greater consumption of whole-grain foods in both girls and boys.

DISCUSSION

The results from this study show that whole grain intake is associated with greater insulin sensitivity and lower BMI in adolescents, particularly for the heaviest children (BMI ≥ 27.5). Adolescents who consumed more than 1½ servings of whole-grain foods per day were leaner and more insulin-sensitive than those who consumed less than ½ serving per day. Compared with lower intake of whole grain, higher intake was also associated with a healthier dietary profile, including greater intakes of fruit and vegetables, fiber, iron, zinc, calcium, folate, and vitamin E.

The effects of whole grain intake on insulin sensitivity have not previously been studied in adolescents. However, feeding studies in adults have shown a beneficial effect of whole grain consumption on glucose tolerance, insulin sensitivity, and satiety, resulting in lower BMI (15–17). In a crossover feeding study among hyperinsulinemic, overweight adult men and women, insulin sensitivity did not change during 4-week periods in which healthy young adults consumed whole-rye versus refined-wheat products (32).

Results from epidemiologic studies have shown a beneficial effect of whole grain consumption on cardiovascular disease risk factors, including lower BMI (12, 13, 30), lower waist circumference or waist:hip ratio, lower total cholesterol level, higher high density lipoprotein cholesterol, and lower prevalences of hypertension and diabetes (12, 17, 30, 32). An inverse dose-response relation was observed between whole grain intake and risk of death from all causes, cardiovascular disease, and cancer in 34,333 women (11, 30). Greater consumption of whole grains was associated with lower risk of coronary heart disease among 75,521 subjects in the Nurses’ Health Study (33).

Results from this study are consistent with studies of adults showing that persons who consume more whole-grain foods appear to have an eating pattern associated with lower cardiovascular disease risk compared with those who consume fewer whole-grain foods (11–13). Because of the
relatively low consumption of whole-grain foods in this adolescent population, we were not able to study the US Dietary Guidelines’ recommendation of three servings of whole grain per day (20). However, our data show that consumption of more than 1/2 servings per day has a significant beneficial effect on body fatness and insulin sensitivity in adolescents. On the basis of the present study, it seems reasonable to suggest that there would be an additional benefit from initiating diets rich in whole-grain foods during childhood and adolescence. Interventions should be designed and promoted to increase the number of whole-grain foods in American diets to improve health. One example of a healthful intervention strategy would be replacement of refined-grain foods, such as white bread and white rice, with whole-grain products, such as whole-wheat bread and brown rice.

Previous reports on this cohort (4) and from other studies (5–7) have shown that insulin resistance is present in adolescence. This emphasizes the importance of promoting healthy eating patterns prior to adulthood. The findings from this study support the 2000 Dietary Guidelines for Americans, which urge them to “eat a variety of grains, especially whole grains” (20).

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REFERENCES


